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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/770,002	01/25/2001	Peter Lloyd Amlot	4-30583A	5207

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EXAMINER
EWOLDT, GERALD R

ART UNIT	PAPER NUMBER
1644	18

DATE MAILED: 04/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/770,002	Amlot et al.
Examiner	**Art Unit**
G.R. Ewoldt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 4, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *4, 5, 8, and 12-15* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *4, 5, 8, and 12-15* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's amendment and remarks, filed 2/02/03, are acknowledged.

2. Claims 1-3, 6, and 9-11 are canceled
Claims 4, 5, 8 and 12-15 are being acted upon.

3. In view of Applicant's amendment, filed 2/04/03, the previous rejection under the second paragraph of 35 U.S.C. 112 has been withdrawn.

4. The specification is objected to for the following informality, "seq id no.", used throughout the specification, is properly SEQ ID NO:. Applicant has not addressed this objection. Failure to address this objection in the next response will be considered non-responsive.
Appropriate correction is required.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 4, 5, 8, and newly added Claims 12-15, stand/are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention, for the reasons of record as set forth in Paper No. 15, mailed 9/05/02.

Applicant arguments, filed 2/04/03, have been fully considered but are not found persuasive. Applicant argues that "the method of treatment defined in amended independent claim 4 does not encompass administering the large genus of CD25 binding molecule [*sic*] to a patient as asserted by the Examiner. Instead, the method of treatment defined in amended independent claim 4 encompasses administering a subgenus of "CD25 binding molecule" having specific features." Applicant continues by arguing that the binding molecules encompassed by the instant claims must comprise defined CDR regions of specific amino acid sequence.

It is the Examiner's position that, as Applicant has disclosed only one embodiment of the antibody of the claims, using only said single embodiment, Applicant cannot accurately estimate the size of the antibody genus of which said antibody is a species. Additionally, chimeric antibodies consist of more than just a collection of amino acid fragments, i.e., CDRs. Antibodies comprise complex three dimensional structures in which the CDRs must fit in precise three dimensional space to create an antibody specific for any particular ligand. It is well-known in the immunological arts that the substituting of CDRs into a random framework is highly unlikely to result in an antibody of the same specificity as that of the antibody from which the CDRs were derived. Chimeric antibodies are actually constructed by trial and error starting with a framework that appears to resemble that from which the CDRs were derived. Accordingly, a written description that consists only of the CDR regions (and in the case of Claims 4, 5, 8, 14, and 15, just half of the CDR regions) is inadequate to describe the CD25 binding molecule of the instant claims.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103 (c)and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 4, 5, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 89/09622 (IDS, of record) in view of Kovarik et al. (1997, of record), for the reasons of record as set forth in Paper No. 15, mailed 9/05/02.

Applicant arguments, filed 2/04/03, have been fully considered but are not found persuasive. Applicant argues that "WO '622 describes anti-TAC chimeric antibodies." However, "WO'622 does not teach or suggest that the specific antibodies recited in amended independent claim 4 can be utilized to treat rheumatoid arthritis." Regarding the Kovarik et al. reference, Applicant argues, "there is no teaching or suggestion in Kovarik et al. that binding of basiliximab to IL-2 receptor at serum concentrations sufficient to saturate the receptor to treat transplant rejection would also be effective to treat rheumatoid arthritis. Accordingly, Kovarik et al. does not remedy deficiencies present in WO '622." And, "It would therefore not have been obvious to a skilled person to combine these separate references and arrive at the subject matter of amended independent claim 4."

It is the Examiner's position that if the '622 document taught that the specific antibodies recited in amended independent claim 4 (basiliximab) could be utilized to treat rheumatoid arthritis, the instant rejection would have been under 102(b). Because the reference did not teach the use of the single antibody of the instant specification (basiliximab) a secondary reference was required and the rejection was made under 103 for obviousness. The reference does teach that "The present invention provides novel compositions useful in the treatment of T-cell mediated human disorders, the compositions containing a chimeric antibody specifically capable of binding to human IL-2 receptors, such as at the epitope bound by the anti-Tac monoclonal antibody. The IL-2 chimeric antibody can have two pairs of light chain/heavy chain complexes, wherein at least one pair has chains comprising mouse variable regions joined with human constant region segments, with or without naturally-associated J and D segments" (page 3) and further teaches rheumatoid arthritis (RA) as one such disease. In other words, the reference teaches the use of a chimeric anti-IL2 receptor antibody for the treatment of RA. Kovarik et al. teaches the chimeric anti-IL2 receptor antibody basiliximab which comprises the CDRs of the instant claims. Accordingly the combined references need comprise nothing more than the substitution of obvious equivalents for a proper obviousness type rejection. However, the Kovarik et al. reference teaches more. It also teaches that basiliximab can achieve IL2 receptor saturation and that the antibody is well tolerated, thus basiliximab could be considered to be not just an equivalent of the antibody of the '622 document, but a *preferred* substitution for said antibody.

Applicant argues that "Additionally, no guidance is provided in the combined prior art that would lead one skilled in the art to pick and choose rheumatoid arthritis out of the long list of diseases recited in WO'622, as the specific disease that can be treated with basiliximab, other than hindsight knowledge of Applicants' invention."

It is clear from the citation at page 3 that the reference teaches the use of an anti-IL2 receptor antibody for the treatment of all T cell-mediated diseases, and what Applicant describes as a "long list" consists of just 5 diseases.

Applicant continues by apparently arguing that the use of basiliximab for the treatment of RA is not enabled by the combined references, "one skilled in the art knowing that factors other than immunological factors are involved in the etiology of rheumatoid arthritis would not be able to reasonably predict that "serum concentrations of basiliximab sufficient to saturate IL-2 receptors" to treat transplant rejection would also be effective to treat rheumatoid arthritis."

This would seem to be a curious argument given the fact that the instant specification provides no data, neither *in vitro* nor *in vivo*, whatsoever. Thus, an argument that the combined references are not enabled, even though they include significant *in vivo* data (the saturation of IL2 receptors) would seem to indicate that the method of the instant claims cannot be enabled either. It is the Examiner's position however, that the combined references do provide an enabling teaching, as peer-reviewed reference teachings must be considered to be at least as enabling as patent specifications, particularly in view of the teaching of IL2 receptor saturation (a measurement which the instant specification discloses as significant). Further, receptor saturation is receptor saturation, whether said saturation is in a transplant patient of an RA patient.

Applicant concludes with the argument that the references do not teach dosing regimens, routes of administration, or duration of treatment.

It must be noted that said dosing regimens, routes of administration, or duration of treatment are only prophetically taught by the specification. Thus, by Applicant's standard, they would not be considered to be enabled. It is the Examiner's position, however, that such parameters comprise only routine

optimization which would fall well within the purview of one of skill in the art.

10. No claim is allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805 The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 at 703-872-9306 (before final) and 703-872-9307 (after final).

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600
April 24, 2003